

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A pharmaceutical composition comprising a mixture of:

- (a) an active macromolecular principle which is a polypeptide or protein, polynucleotide or polysaccharide;
- (b) a non-conjugated bile acid or salt; and
- (c) an additive chosen from
 - (i) propyl gallate or a linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester of gallic acid which is optionally substituted with one or more groups which are the same or different and are selected from halogen and α-linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl-ester;
 - (ii) butyl hydroxy anisole, or butylhydroxy anisole wherein the methyl group or the methoxy group linked to the aromatic ring and/or the hydrogen ortho to the hydroxyl group is/are replaced by one or more groups which are the same or different and are selected from linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio and C₂₋₁₂ alkenyl, either unsubstituted or substituted in any position by one or more halogen atoms; and
 - (iii) a mixture of (i) and (ii)

wherein the mixture comprises at least 1% by weight of the additive (c) and wherein the composition, when introduced into the intestine, does not raise the pH of the intestinal fluid above pH 7.5~~the composition is coated with an enteric coating which becomes permeable at a pH from 3 to 7.~~

2. (original) A composition according to claim 1, which comprises less than 5% by weight of water.

3.-4 (canceled).

5. (currently amended) A composition according to claim 1, wherein the ratio by weight of the non-conjugated bile salt+additive (b + c) to the ~~polypeptide or proteinactive macromolecular principle~~ is at least 5:1.

6. (previously presented) A composition according to claim 1, wherein the mixture is in the form of a solution or a microparticulate dispersion.

7. (previously presented) A composition according to claim 1, wherein the mixture is in solid form.

8. (canceled).

9. (currently amended) A composition according to claim 1, where the ~~polypeptide or proteinactive macromolecular principle~~ is chosen from insulin, calcitonin, growth hormone, parathyroid hormone, erythropoietin, GLP1 and GCSF, and derivatives and analogues thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin, or is single, double or triple-stranded RNA.

10. (currently amended) A composition according to claim 9, where the ~~polypeptide or protein active macromolecular principle~~ is insulin, calcitonin, parathyroid hormone or a derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.

11. (currently amended) A composition according to claim 10, wherein the ~~polypeptide or protein active macromolecular principle~~ is insulin or a derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin, and the composition further comprises an insulin sensitizing agent.

12. (previously presented) A composition according to claim 1, wherein component (b) is chenodeoxycholate.

13. (currently amended) A composition according to claim 1, wherein the additive is chosen from propyl gallate or an analogue or a derivative thereof, including esters of gallic acid, where the esters may be linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester, ester of gallic acid which is, and the compounds are optionally substituted with one or more groups which are the same or different and are selected from halogen, and linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl esters.

14. (currently amended) A composition according to claim 1, wherein the additive is chosen from BHA or an analogue or derivative thereof, including analogues and derivatives of butyl hydroxy anisole or hydroxy anisole where the methyl group or the methoxy group linked to the

aromatic ring and/or the hydrogen ortho to the hydroxyl group are replaced by linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl, either unsubstituted or substituted in any position, especially by one or more halogen atoms.

15.-18. (canceled).

19. (currently amended) A method according to claim 26 wherein the polypeptide or protein active macromolecular principle to be absorbed is chosen from insulin, calcitonin, growth hormone, parathyroid hormone, erythropoietin, GLP1 and GCSF, and derivatives and analogues thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin, or is single, double or triple-stranded RNA.

20. (currently amended) A method according to claim 19, wherein the polypeptide or protein active macromolecular principle to be absorbed is insulin, calcitonin, parathyroid hormone or a derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.

21. (currently amended) A method according to claim 20, wherein the polypeptide or protein active macromolecular principle to be absorbed is insulin or a derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin, and an insulin sensitizing agent is also present.

22. (previously presented) A method according to claim 26, wherein the composition comprises less than 5% by weight of water.

23. (currently amended) A method according to claim 26, wherein the polypeptide or protein inactive macromolecular principle which is a polypeptide or protein, polynucleotide or polysaccharide, the non-conjugated bile acid or salt and the additive are formulated as a solution, a microparticulate dispersion or a solid.

24. (currently amended) A method of enhancing the absorption of a polypeptide or protein inactive macromolecular principle in a patient, which method comprises administering to said patient a composition as defined in claim 1.

25. (canceled).

26. (currently amended) A method of enhancing the absorption of polypeptides or proteins an active macromolecular principle which is a polypeptide or protein, polynucleotide or polysaccharide across the intestinal wall in a human or animal body, which method comprises administering a non-conjugated bile acid or salt, together with an additive chosen from:

- (i) propyl gallate or a linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester of gallic acid which is optionally substituted with one or more groups which are the same or different and are selected from halogen and a linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester;

- (ii) butyl hydroxy anisole, or ~~butyl~~ hydroxy anisole wherein the methyl group or the methoxy group linked to the aromatic ring and/or the hydrogen *ortho* to the hydroxyl group is/are replaced by one or more groups which are the same or different and are selected from linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio and C₂₋₁₂ alkenyl, either unsubstituted or substituted in any position by one or more halogen atoms; and
- (iii) a mixture of (i) and (ii)

together with the ~~polypeptide or protein~~ inactive macromolecular principle in a pharmaceutical composition, wherein the additive accounts for at least 1% by weight of the total weight of (a) the ~~polypeptide or protein~~ inactive macromolecular principle, (b) the non-conjugated bile acid or salt, plus (c) the additive, and wherein the composition, when introduced into the intestine, does not raise the pH of the intestinal fluid above pH 7.5, the composition is coated with an enteric coating which becomes permeable at a pH from 3 to 7, and which method enhances the absorption of the ~~polypeptides or proteins~~ inactive macromolecular principle due to the additive improving the solubility of the bile salt.

27. (currently amended) A pharmaceutical composition according to claim 431, wherein the enteric coating becomes permeable at a pH from 5.5 to 7.

28. (previously presented) A pharmaceutical composition according to claim 27, wherein the enteric coating becomes permeable at a pH from 5.5 to 6.5.

29. (currently amended) A method according to claim 2632, wherein the enteric coating becomes permeable at a pH from 5.5 to 7.

30. (previously presented) A method according to claim 29, wherein the enteric coating becomes permeable at a pH from 5.5 to 6.5.

31. (new) A method according to claim 1, wherein the composition is coated with an enteric coating which becomes permeable at a pH from 3 to 7.

32. (new) A method according to claim 26, wherein the composition is coated with an enteric coating which becomes permeable at a pH from 3 to 7

33. (new) A composition according to claim 1, wherein the composition, when introduced into the intestine, enhances absorption of the active macromolecular principle due to the additive improving solubility of the bile salt.

34. (new) A composition according to claim 1, wherein the composition, when introduced into the intestine, does not raise the pH of the intestinal fluid above pH 7.

35. (new) A method according to claim 26, wherein the composition, when introduced into the intestine, does not raise the pH of the intestinal fluid above pH 7.